

Results of patch testing with a special series of rubber allergens

D. LINN HOLNESS¹ AND JAMES R. NETHERCOTT²

¹Department of Occupational and Environmental Health, St Michael's Hospital, University of Toronto, Canada

²Department of Dermatology, University of Maryland, USA

The purpose of this study was to examine the results of patch testing with the rubber components on a standard screening tray and compare them with the results of testing with a special series of 27 rubber components (rubber tray). 1670 patients were patch tested with the screening tray and 317 of these were also tested with the rubber tray. 16% of those tested with the rubber tray had a positive response to at least 1 of the rubber allergens on the screening tray and 22% had a positive response to at least 1 of the allergens on the rubber tray. The most common positive response to the rubber tray allergens was to tetramethylthiuram monosulfide. There were no responses to 3 of the components on the rubber tray and there was only 1 positive response to a further 4 components. The diagnostic test characteristics of the rubber components on the screening tray were examined using the rubber tray as the gold standard. The sensitivity of the screening tray was 94%, specificity 51%, positive predictive value 87% and negative predictive value 71%. Of the 317 tested, 11% were found to have a positive to a substance on the rubber tray that was not evident from the results of the screening tray.

Key words: patch testing technique; allergic contact dermatitis; rubber allergens; false-negative reactions; false-positive reactions. © Munksgaard, 1997.

Accepted for publication 30 December 1996

Physicians carrying out patch testing often use special series of allergens in addition to a screening tray. Although these special series of allergens are used, there is relatively little information in the literature on the results obtained when using these trays. While a number of investigators have reported their experience with rubber-related allergic contact dermatitis (ACD), there is little information regarding the results of testing with special series of rubber allergens. The information in the literature largely consists of patch test clinic results, which include information about those with positives to various rubber mixes, the usefulness of the rubber mixes, industry-based surveys and case reports (1–15). There is relatively little information in the literature related to the diagnostic test characteristics of either a special series of rubber allergens or the related allergens on the screening tray. With increasing attention being paid to the diagnostic performance of various testing procedures, concerns about quality of care and fiscal resource implications of various test methodologies, it is timely to consider this issue further, as it relates to patch testing.

The objectives of the current study were to examine the characteristics of those tested with the rubber tray in our Clinic, to examine the results of testing with the rubber tray, and to examine the test performance of rubber allergens on the standard screening tray in comparison with the rubber tray.

Material and Methods

When the Clinic was first started, patch testing was carried out using the European standard series as the routine screening tray. Since 1985, the North American Contact Dermatitis Group standard screening tray was used. The allergens used for patch testing were supplied by either Hermal (Kurt Herrmann, Rhinebeck, Germany), Trolle Larsen (Copenhagen, Denmark) or Chemotechnique Diagnostic Limited (Malmo, Sweden).

In each case, the patients were patch tested with either Al-test strips (Imeco AB, Sweden) or Finn Chambers (Epitest Limited OY, Finland). The patch test strips were applied to the subject's back using Scanpor tape (Norgesplaster, Norway) and

left in place for 2 or 3 days. The initial reading took place 30 to 60 min after the patch tests were removed. A second reading was made at 2 or 3 days following the first reading. The scoring methods were those used by the International Contact Dermatitis Group, as previously described (8).

The patch test results were recorded on standardized forms. Demographic information, including diagnosis, distribution of the eruption, job, past history of atopic disease, length of time of the skin problem, and the use of protective equipment were also used in the analysis. Initially, this information was abstracted from the written notes in the clinic chart. As time progressed, standardized collection sheets for this information were developed, and in the latter years were used to collect this information.

Table 1. Characteristics of those tested with rubber tray versus those not tested with the rubber tray (% unless otherwise noted)

	Rubber tray		<i>p</i> -value
	no (<i>n</i> =1353)	yes (<i>n</i> =317)	
age – years	40.0	39.4	0.648
rash time – months	40	43	0.495
sex – female	49	32	0.001
past history			
allergy	30	25	0.092
hayfever	21	23	0.589
asthma	6	10	0.078
eczema	13	9	0.148
atopy	38	35	0.330
family history			
allergy	18	16	0.694
hayfever	16	21	0.118
asthma	12	10	0.453
eczema	15	13	0.445
atopy	31	31	0.957
diagnosis			
allergic CD	36	45	0.005
irritant CD	23	36	0.001
atopic dermatitis	12	11	0.844
occupational	44	74	0.000
location			
general	7	4	0.068
hands	53	79	0.001
feet	8	14	0.001
face	19	7	0.001
eyelids	11	3	0.001
neck	7	1	0.001
arm	23	27	0.166
leg	10	8	0.255
trunk	9	6	0.149
job characteristics			
health care worker	3	6	0.006
type: not working	13	10	
office	26	10	
wet work	18	25	0.001
industrial	43	56	
use gloves	26	70	0.001

Table 2. Results of standard screening tray comparing those tested with rubber tray with those not tested with rubber tray (% positive)

Allergen	Rubber tray		<i>p</i> -value
	no (<i>n</i> =1353)	yes (<i>n</i> =317)	
balsam Peru 25%	5.1	3.8	0.352
benzocaine 5%	0.6	0.0	0.296
benzyl peroxide 1%	1.1	2.1	0.320
black rubber mix 0.6%	1.8	2.0	0.818
carba mix 3%	3.4	4.8	0.254
cinnamic alcohol 5%	5.3	2.7	0.199
cinnamic aldehyde 1%	3.6	5.5	0.281
cobalt 1%	7.1	10.0	0.131
diaminophenylmethane 1%	2.4	4.1	0.237
epoxy 1%	3.9	2.7	0.332
ethylenediamine 1%	3.9	6.7	0.035
formaldehyde 1%	6.2	8.7	0.292
formaldehyde 2%	7.6	8.4	0.737
fragrance mix 8%/16%	20.8	15.4	0.168
mercapto mix 1%	0.9	2.8	0.071
mercapto mix 2%	1.4	3.3	0.113
mercaptobenzothiazole 1%	0.9	3.5	0.018
neomycin 20%	4.2	3.0	0.343
nickel sulphate 2.5%	12.2	11.7	0.873
nickel sulphate 5%	9.8	9.2	0.823
paraben mix 15%	2.2	2.6	0.782
paraphenylenediamine 1%	6.9	4.8	0.189
PTBphenylformaldehyde			
resin 1%	1.3	1.2	0.916
potassium dichromate 0.25%	4.6	5.5	0.651
potassium dichromate 0.5%	7.5	6.5	0.661
quaternium-15 1%/2%	5.2	3.4	0.365
rosin 20%	4.8	2.7	0.139
rosin 60%	3.3	2.8	0.803
thiomerosal 0.1%	3.2	5.5	0.179
thiuram mix 1%	3.8	8.8	0.001
wool wax alcohol 30%	1.5	1.4	0.829

All of the data was entered into a dBase file, and analyzed on the University of Toronto computer system using SAS (16). Basic descriptive information, including frequencies, means and standard deviations, were calculated. Comparisons between groups were carried out using χ^2 or logistic regression analysis for binary data, and *t*-tests or multiple regression analysis for continuous data. A *p*-value of 0.05 was considered to be statistically significant.

Results

The main dataset examined contained 1,670 patients patch tested between 1981 and 1988. The results of the screening tray indicated that 8.9% of the individuals had a positive response to at least 1 of the rubber components on the tray. 50% of these had a positive to thiuram mix, 38% to carba mix, 20% to black rubber mix, 15% to mercapto mix and 14% to mercaptobenzothiazole.

Next, analysis was carried out to determine the characteristics of those 317 individuals who had been tested with the rubber tray and compare them to those who were not tested with the specialized tray (Tables 1, 2). Individuals tested with the rubber tray were more likely to be male, use gloves, report dermatitis of the hands or the feet and less likely to report generalized involvement or involvement of the face, eyelids and neck. They were more likely to be health care workers and less likely to be office workers. When the results of the standard screening tray were compared, those who were tested with the specialized tray were more likely to have positive responses to a variety of rubber components, including mercaptobenzothiazole,

Table 3. Rubber tray allergens (n=317)

Allergen	no. tested	% positive
monobenzene 1%	178	0.6
4,4 dihydroxybiphenyl 0.1%	311	1.0
hexamethylenetetramine 2%	309	1.9
mercaptobenzothiazole 1%/2%	316	3.5
dibenzylthiazyl disulphide 1%	309	1.9
diphenylthiourea 1%	176	0.0
ethylenethiourea 1%	176	0.6
dithiodimorpholine 1%	176	0.0
dibutylthiourea 1%	176	1.1
diethylthiourea 1%	176	1.1
n-cyclohexylbenzothiazyl sulfenamide 1%	316	1.6
1,3 diphenylguanidine 1%	316	4.4
N-isopropyl-N-phenyl paraphenylenediamine 0.1%	316	2.8
tetramethylthiuram monosulfide 0.25%/1%	315	6.0
bis(diethyldithiocarbamate) zinc 1%	317	2.2
tetramethylthiuram disulfide 0.25%/1%	316	3.8
N-Cyclo-hexyl-N-phenyl phenylenediamine 1%	316	2.5
N,N-diphenyl paraphenylenediamine 0.25%/1%	316	1.6
morpholinylmercaptobenzothiazole 0.5%/1%	316	2.8
tetraethylthiuram disulfide 0.25%/1%	316	2.8
dipentamethylenethiuram disulfide 1%	316	1.9
bis(dibutylthiocarbamate) zinc 1%	317	1.3
cyclohexyl thiophthalimide 1%	94	3.2
piperazine 1%	93	3.2
N,N dibeta naphthyl 4 phenylenediamine 1%	220	1.4
N-phenyl-2 naphthylamine 1%	220	0.0
mercaptobenzimidazole X%	148	0.7

Table 4. Correlation between rubber positives on screening and rubber trays

		Screening tray	
		negative	positive
Rubber tray	negative	231	15
	positive	35	36

sensitivity=94.

specificity=51.

positive predictive value=87.

negative predictive value=71.

Table 5. Characteristics of false negatives to rubber allergens on the screening tray (% unless otherwise noted)

	False negatives		p-value
	no (n=302)	yes (n=15)	
age – years	39.3	40.1	0.759
rash time – months	46	19	0.001
sex – female	34	20	0.102
use gloves	69	77	0.405
past history			
allergy	24	27	0.754
hayfever	24	14	0.316
asthma	10	10	0.976
eczema	10	5	0.416
atopy	35	33	0.864
family history			
allergy	15	25	0.326
hayfever	19	38	0.079
asthma	9	19	0.198
eczema	13	17	0.625
atopy	30	39	0.450
diagnosis			
allergic CD	40	86	0.001
irritant CD	38	14	0.005
atopic dermatitis	12	6	0.265
occupational	72	83	0.164
location			
general	4	6	0.610
hands	79	80	0.861
feet	14	14	0.941
face	7	6	0.709
eyelids	3	3	0.995
neck	1	0	0.478
arm	27	29	0.803
leg	7	17	0.031
trunk	6	9	0.559

thiuram mix, and mercapto mix, and also to ethylenediamine.

317 individuals were patch tested with the rubber tray. 16% of those tested with the specialized rubber tray had a positive response to at least 1 rubber component on the screening tray. 22% of 317 tested with the rubber tray had a positive response to at least 1 of the rubber allergens on the rubber tray.

The specific results of the rubber tray involved 27 components (Table 3). 3 substances had no positive responses, and for 4 substances there was only 1 positive response.

The test performance of the screening tray rubber components was compared with the results of the specialized rubber tray for these 317 individuals (Table 4). The rubber tray was taken to be the “gold standard” and the diagnostic test under consideration was the rubber components on the screening tray. The test characteristics for the rubber components on the screening tray included a sensitivity of 94%, specificity of 51%, positive pre-

dictive value of 87%, and negative predictive value of 71%. 11% of individuals who were positive on the rubber tray did not have a positive response to rubber allergens on the screening tray.

The 15 individuals who had false-negative responses on the standard screening tray (i.e. negative to screening tray but positive on rubber tray) tended to be individuals who had a shorter duration of the rash (Table 5) and were more likely to have involvement of the legs. They were more likely to be positive to hexamethylenetetramine, diphenylguanidine, cyclohexyl thiophthalimide and PPD-related materials. These materials are ones which have been less likely to be picked up on the standard screening tray aside from the PPD-related materials.

The 35 individuals who had false-positive responses on the standard screening tray (i.e., positive to rubber allergen on screening tray but no positive responses to rubber tray) were more likely to be females, individuals using gloves, and atopics (Table 6). There was a statistically significant in-

Table 6. Characteristics of false positives to rubber allergens on the screening tray (% unless otherwise noted)

	False positives		<i>p</i> -value
	no (<i>n</i> =282)	yes (<i>n</i> =35)	
age – years	39.4	39.9	0.895
rash time – months	42	66	0.508
sex – female	31	53	0.072
use gloves	69	100	0.016
past history			
allergy	24	42	0.156
hayfever	21	50	0.023
asthma	9	17	0.411
eczema	8	33	0.003
atopy	34	58	0.081
family history			
allergy	15	40	0.037
hayfever	19	40	0.118
asthma	10	10	0.973
eczema	11	40	0.009
atopy	29	60	0.042
diagnosis			
allergic CD	43	73	0.023
irritant CD	36	33	0.848
atopic dermatitis	11	13	0.805
occupational	73	67	0.569
location			
general	4	7	0.608
hands	78	93	0.160
feet	14	13	0.950
face	7	7	0.928
eyelids	3	0	0.498
neck	1	0	0.654
arm	26	40	0.238
leg	8	13	0.423
trunk	7	0	0.303

Table 7. Results of screening tray patch testing in those with false positives to rubber allergens on the screening tray (% unless otherwise noted)

<i>Allergen</i>	False Positives		<i>p</i> -value
	no (<i>n</i> =282)	yes (<i>n</i> =35)	
balsam Peru 25%	3	13	0.048
benzocaine 5%	0	0	–
benzoyl peroxide 1%	1	20	0.004
black rubber mix 0.6%	2	0	0.566
carba mix 3%	3	47	0.001
cinnamic alcohol 5%	2	20	0.016
cinnamic aldehyde 1%	5	20	0.147
cobalt 1%	10	15	0.505
diaminophenylmethane 1%	4	0	0.636
epoxy 1%	2	7	0.331
ethylenediamine 1%	6	20	0.035
formaldehyde 2%	8	20	0.174
fragrance mix 8%/16%	13	50	0.005
mercapto mix 1%	2	20	0.017
mercapto mix 2%	3	10	0.213
mercaptobenzothiazole 1%	3	20	0.042
neomycin 20%	3	0	0.481
nickel sulfate 2.5%	11	40	0.045
nickel sulfate 5%	10	0	0.299
paraben mix 15%	15	50	0.204
paraphenylenediamine 1%	5	0	0.373
PTBphenylformaldehyde resin 1%	1	14	0.001
potassium dichromate 0.25%	6	0	0.584
potassium dichromate 0.5%	6	10	0.642
quaternium-15 1%	12	0	0.603
rosin 20%	2	8	0.253
thimerosal 0.1%	6	0	0.582
thiuram mix 1%	8	33	0.001
wool wax alcohol 30%	1	0	0.642

crease in the frequency of positive responses to 7 of the 23 non-rubber allergens on the standard screening tray in this group (Table 7). Therefore, those with a false-positive response to the screening tray seemed to be individuals who were more likely to have positive responses to a number of allergens on the standard screening tray in addition to rubber. Labourers, health care workers, construction workers and automotive workers were over-represented in the group of false positives.

Discussion

A number of others have reported the results of using a variety of rubber components. Most of the information relates to the rubber mixes used on the screening trays. Other authors have generally found between a 3.8% and 15.7% positive response to the various rubber components used on a screening tray. A value of 8.9% would be consistent with the findings of others. With respect to the specific materials identified, other studies have generally found a greater proportion to be positive to

thiuram mix, usually between 70 and 80%, and a lesser number positive to carba mix.

The test characteristics of the rubber allergens on the screening tray were generally good, and suggest it to be a useful test. Given the need to consider health care costs, it appears appropriate that, for most individuals, use of the screening tray alone is appropriate if one is considering a rubber allergy, particularly if it is thought to be related to glove use. In those individuals who have other exposures to rubber, such as in an industrial setting, use of the specialized tray with the wider selection of rubber allergens may be indicated. In those individuals who are negative to the standard screening tray, but for whom there is still a very strong suspicion of an allergic contact, secondary testing with a specialized collection of rubber allergens could be undertaken. However, there is not convincing evidence from this study that there is much to be gained from initially patch testing all individuals with possible glove-related rubber allergy to the specialized rubber tray. In the instance of a glove-related allergy, it is usually not important to know which specific type of, for example, thiuram, is the problem; rather that it is thiuram, so a thiuram-containing glove may be avoided. In the case of a specialized industrial process, this issue may be more important, or it may be important for a specific compensation purpose, where it is necessary to demonstrate an allergy to a specific compound in the workplace. In these instances, initial testing with the rubber tray is probably indicated. It is also suggested that the possible relevance of positive responses to rubber allergens on the screening tray might be questioned if the individual has a number of other positive responses.

References

1. Condé-Salazar L, Del-Rio E, Guimaraens D, Gonzalez Domingo A. Type IV allergy to rubber additives: a 10-year study of 686 cases. *J Am Acad Dermatol* 1993; 29: 176-180.
2. Von Hintzenstern J, Heese A, Koch U, Peters K-P, Hornstein O P. Frequency, spectrum and occupational relevance of type IV allergies to rubber chemicals. *Contact Dermatitis* 1991; 24: 244-252.
3. Fousseureau J, Menezes-Brandão F, Cavalier C, Herve-Bazin B. Allergy to MBT and its derivatives. *Contact Dermatitis* 1983; 9: 514-516.
4. Lynde C W, Mitchell J C, Adams R M, Maibach H I et al. Patch testing with mercaptobenzothiazole and mercaptomixes. *Contact Dermatitis* 1982; 8: 273-274.
5. Mitchell J C. Patch testing with mixes: note on mercaptobenzothiazole mix. *Contact Dermatitis* 1981; 7: 98-104.
6. Themido R, Bradnao F M. Contact allergy to thiurams. *Contact Dermatitis* 1984; 10: 251.
7. Menne T, White I R, Bruynzeel D P, Dooms-Goossens A. Patch test reactivity to the PPD-black-rubber-mix (industrial chemicals) and individual ingredients. *Contact Dermatitis* 1992; 26: 354.
8. Nethercott J R, Holness D L, Adams R M et al. Patch testing with a routine screening tray in North America, 1985-1989 (I). Frequency of response. *Am J Contact Dermatitis* 1991; 2: 122-129.
9. Holness D L, Nethercott J R. Patch testing in an occupational health clinic. *Am J Contact Dermatitis* 1994; 5: 150-155.
10. Riboldi A, Lobaccaro M. Occupational contact dermatitis from rubber. *Clinics in Dermatology* 1992; 10: 149-155.
11. White I R. Dermatitis in rubber manufacturing industries. *Dermatol Clin* 1988; 6: 53-59.
12. Varigos G A, Dunt D R. Occupational dermatitis. An epidemiological study in the rubber and cement industries. *Contact Dermatitis* 1981; 7: 105-110.
13. Zina A M, Bedello P G, Cane D, Bundino S, Benedetto A. Dermatitis in a rubber tyre factory. *Contact Dermatitis* 1987; 17: 17-20.
14. Ancona A, Monroy F, Fernandez-Diez J. Occupational dermatitis from IPPD in tyres. *Contact Dermatitis* 1982; 8: 91-94.
15. Kilpikari I. Occupational contact dermatitis among rubber workers. *Contact Dermatitis* 1982; 8: 359-362.
16. SAS Institute Inc. *SAS user's guide: statistics*. SAS Institute Inc, Cary, North Carolina, 1985.

Address:

D. L. Holness
Department of Occupational Health
St Michael's Hospital
30 Bond St
Toronto, Ontario
Canada, M5B 1W8

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.